### **National Center for Immunization & Respiratory Diseases**



# Influenza Disease Burden, Vaccine Benefits, and Current Vaccine Recommendations

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## **Summary Points**

- Influenza activity increases seasonally in the U.S. each year, generally from fall through early spring (though timing varies year to year).
- Influenza severity and illness burden vary from season to season.
- Older adults, young children, pregnant persons, immunocompromised persons, and those
  with certain chronic medical conditions are among those at increased risk of
  severe/complicated illness.
- Routine vaccination has been recommended for some populations since 1960, and for all aged ≥6 months since 2010.
- Influenza vaccine effectiveness varies, depending upon factors such as age and health of the recipient and "match" between vaccine and circulating viruses.
- Even in a season of modest vaccine effectiveness, influenza vaccination can prevent substantial disease burden (illnesses, hospitalizations, and deaths).

# Influenza Disease Burden

## **Influenza Complications**

### Moderate Illness:

- Otitis media (in young children), sinusitis.
- Exacerbation of chronic disease.

### Severe to Critical Illness:

- Exacerbation of chronic disease.
- Respiratory: viral pneumonia, croup, status asthmaticus, bronchiolitis, tracheitis,
   Acute Respiratory Distress Syndrome.
- Cardiac: myocarditis, pericarditis, myocardial infarction.
- Neurologic: encephalopathy & encephalitis, stroke, Guillain-Barre syndrome
   (GBS), Acute Disseminated Encephalomyelitis (ADEM), Reye syndrome.
- Bacterial co-infections (e.g. pneumonia).
- Musculoskeletal: myositis, rhabdomyolysis.
- Multi-organ failure (respiratory, renal failure, septic shock).
- Healthcare-associated infections (e.g. ventilator-associated pneumonia).

# **Groups at Increased Risk for Influenza Complications and Severe Illness**

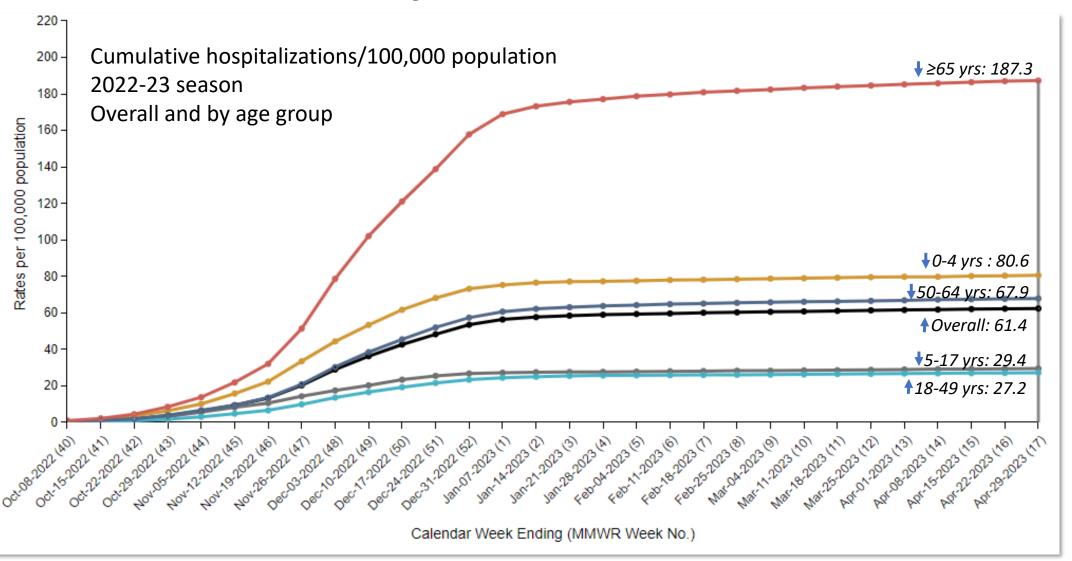
- Children under 5 years and adults aged 65 years and older.
- Persons with chronic medical conditions, including pulmonary (including asthma) or cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic (including persons who have had a stroke) and neurodevelopmental, hematologic, metabolic or endocrine disorders (including diabetes mellitus).
- Persons who are immunocompromised.
- Persons with extreme obesity (BMI ≥40).
- Children and adolescents who are receiving aspirin-or salicylate-containing medications (who might be at risk for Reye syndrome after influenza virus infection).
- Residents of nursing homes and other long-term care facilities.
- Pregnant persons and people up to 2 weeks postpartum.
- People from certain racial and ethnic minority groups, including non-Hispanic Black, Hispanic or Latino, and American Indian or Alaska Native persons.

### **CDC Influenza Surveillance**

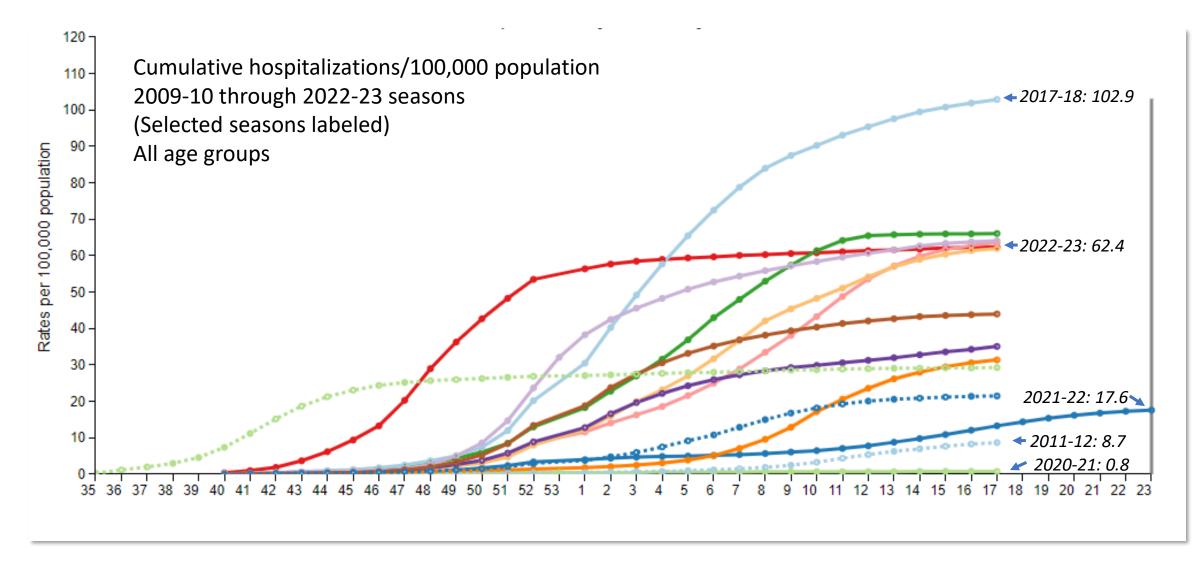


- Weekly U.S. Influenza Surveillance Report: <a href="https://www.cdc.gov/flu/weekly/index.htm">https://www.cdc.gov/flu/weekly/index.htm</a>.
- Includes data from several systems examining various aspects of influenza activity (e.g., characteristics of circulating viruses; surveillance of outpatient illnesses, hospitalizations, and deaths).
- We'll focus here on two indices of severe illness: hospitalizations and deaths.

## Influenza-Associated Hospitalizations—FluSurv-NET



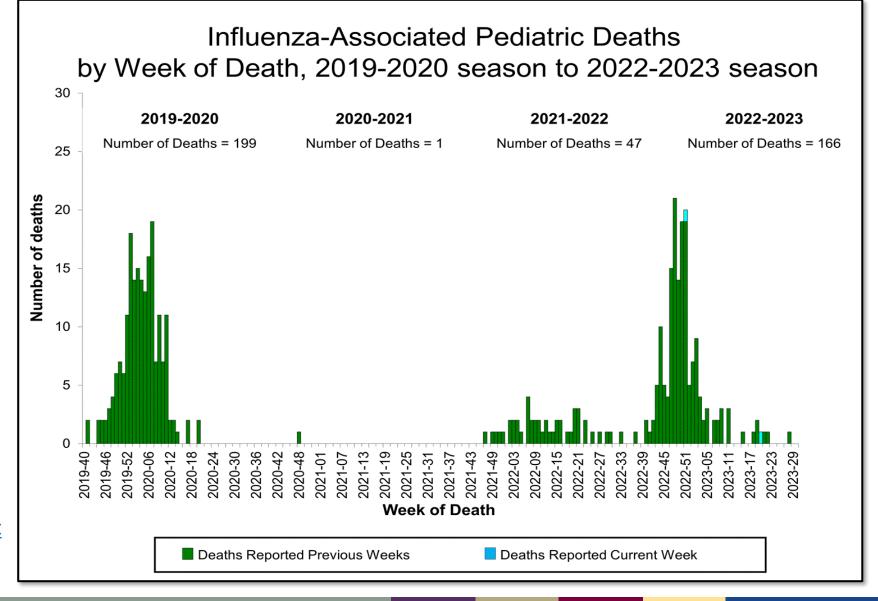
## Influenza-Associated Hospitalizations—FluSurv-NET



## Pediatric Influenza Mortality Surveillance

- Pediatric deaths
   associated with lab confirmed influenza are
   reportable since 2004.
- Approx. 50% of deaths occur in children with no risk factors for severe influenza illness.
- Each season, approx.
   80% of those eligible for vaccination were not vaccinated for the season.

Weekly U.S. Influenza Surveillance Report | CDC Flannery et al. Pediatrics 2017;139(5); e20164244.



### **Annual Influenza Burden Estimates**

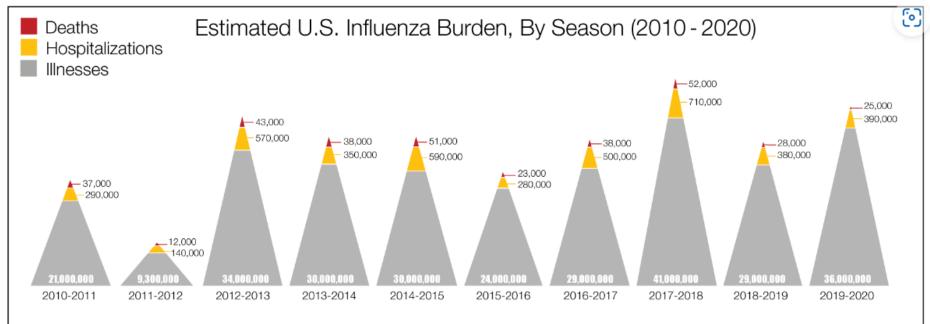
While not all seasonal influenza is reportable, influenza burden can be estimated using modeling methods, including information drawn from:

- Surveillance data
- Testing practices
- Test characteristics
- Death certificate data

Disease Burden of Flu | CDC

From 2010-11 through 2021-22, estimated annual influenza burden ranged from:

Deaths 12,000-52,000 Hospitalizations 140,000-710,000 Illnesses 9,000,000-41,000,000



## U.S. Influenza Vaccination Recommendations

## Surgeon General Recommendation for Routine Influenza Vaccination of Civilians, 1960

#### Vaccination recommended for:

- Persons of any age with chronic debilitating conditions.
- Pregnant women.
- All persons aged 65 years or older.

Burney LE.
Public Health Rep. 1960 Oct;75(10):944.

#### STATEMENT

By Leroy E. Burney, Surgeon General, Public Health Service

#### Influenza Immunization

Two outbreaks of influenza swept the United States in the fall of 1957 and the winter of 1958, resulting in 60,000 more deaths than would be expected under normal conditions. There were, in addition, more than 26,000 excess deaths during the first 3 months of 1960 which also were considered to be the result of influenza.

These departures from the usually predictable norms prompted the Surgeon General's Advisory Committee on Influenza Research to analyze the cause and to seek measures to prevent such an occurrence in the future.

The committee found that a new antigenic variant, the Asian strain, because of its wide-spread introduction and the general lack of resistance to it, was the direct cause of the excess number of deaths, not only in the total population but most markedly among the chronically ill, the aged, and pregnant women. As a result of these findings, the Public Health Service is urging a continuing program to protect these high-risk groups in order to prevent a recurrence of this excess mortality.

The high-risk groups who contribute most to the excess deaths and who the Public Health Service believes should be routinely immunized

- 1. Persons of all ages who suffer from chronic debilitating disease, in particular: (a) rheumatic heart disease, especially mitral stenosis; (b) other cardiovascular diseases, such as arteriosclerotic heart disease or hypertension—especially patients with evidence of frank or incipient insufficiency; (c) chronic bronchopulmonary disease, for example, chronic asthma, chronic bronchitis, bronchicetasis, pulmonary fibrosis, pulmonary emphysema, or pulmonary tuberculosis; (d) diabetes mellitus; (e) Addison's disease.
- 2. Pregnant women.
- 3. All persons 65 years or older.

The adult dosage recommended by the advisory committee for initial immunization is 1.0 cc. (500 cca units) of polyvalent vaccine, administered subcutaneously on two occasions separated by two or more months. Preferably, the first dose would be given no later than September 1 and the second no later than November 1. Persons previously immunized with polyvalent vaccine should be reinoculated with a single booster dose of 1.0 cc. subcutaneously each fall, prior to November 1. The only contraindication to vaccination would be a history of food allergy to eggs or chicken or a prior history of allergic reaction to an eggproduced vaccine, such as the commercial influenza product.

The time to start such a program is before the onset of the influenza season this fall. In the past, influenza vaccination has been sparse and sporadic, and primarily in response to an epidemic or the threat of an epidemic. The unpredictability of recurrence of influenza and its continued endemic occurrence are well known. Therefore, the Public Health Service strongly recommends that immunization of these high-risk groups be started now and continued annually, regardless of the predicted incidence of influenza for specific years.

The members of the Surgeon General's Advisory Committee on Influenza Research are: Colin M. MacLeod, M.D., chairman, University of Pennsylvania, Fred M. Davenport, M.D., University of Michigan, Morris Schaeffer, M.D., bureau of laboratories of the City of New York Health Department, George Burch, M.D., Tulane University, Dorland J. Davis, M.D., National Institute of Allergy and Infectious Diseases, Public Health Service, Thomas F. Sellers, M.D., Georgia State Department of Health, and Glenn S. Usher, M.D., Communicable Disease Center, Public Health Service.

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944 Public Health Reports

Ages ≥65 years

Pregnant women 2<sup>nd</sup>/3<sup>rd</sup> trimester

Any age with chronic medical conditions

Contacts of recommended groups

Health care personnel

# ACIP Influenza Vaccine Recommendations Expansion, 2000-2010

+ Healthy children ages 6-23 months

+ Healthy children ages 24-59 months

+ Healthy
adults ages 1949 years—
Vaccination
recommended
for all ≥6
months

Pre-2000

2000

2003

2004

2006

2008

2010

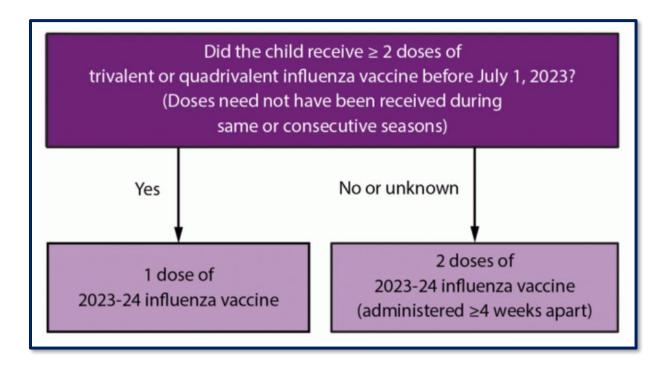
+ Healthy adults ages 50-64 years

Pregnant women in all trimesters

+ Healthy children ages 5-18 years

### **Annual Influenza Vaccination**

- Recommended for all ages 6 months and older who do not have contraindications.
- Children 9 years and older and adults need one dose for the season.
- Some children ages 6 months through 8 years need two doses:
  - If they have not received a total of ≥2 doses by the July 1 prior to the start of the season,
  - Or, if their influenza vaccination history is unknown.



Prevention and Control of Seasonal Influenza with Vaccines:

Recommendations of the Advisory Committee on

Immunization Practices — United States, 2023—24 Influenza
Season | MMWR (cdc.gov)

### **Influenza Vaccine Types**

- Currently 3 vaccine types (inactivated, recombinant, live attenuated); 9 brands.
- Inactivated vaccines include standard dose unadjuvanted, high-dose unadjuvanted, and standard-dose adjuvanted.
- All are quadrivalent (contain 1 A(H1N1), 1 A(H3N2), 1 B/Victoria, 1 B/Yamagata).
- Approved ages vary; none are approved for under age 6 months.
- Any age-appropriate vaccine can be used.
  - Live attenuated vaccine not recommended in pregnancy or for those with some medical conditions
  - No preferential recommendations for persons ages 6 months through 64 years.
  - High-dose inactivated, recombinant, and adjuvanted inactivated are preferred for ages ≥65 years.

Pre-2003-04: Standard-dose inactivated (egg-based) 2003-04: Live attenuated (nasal spray; egg-based)

2010-11:
High-dose
inactivated
(egg-based)

2013-14: Cell culture inactivated and Recombinant (nonegg-based)

2016-17 adjuvanted inactivated (egg-based)

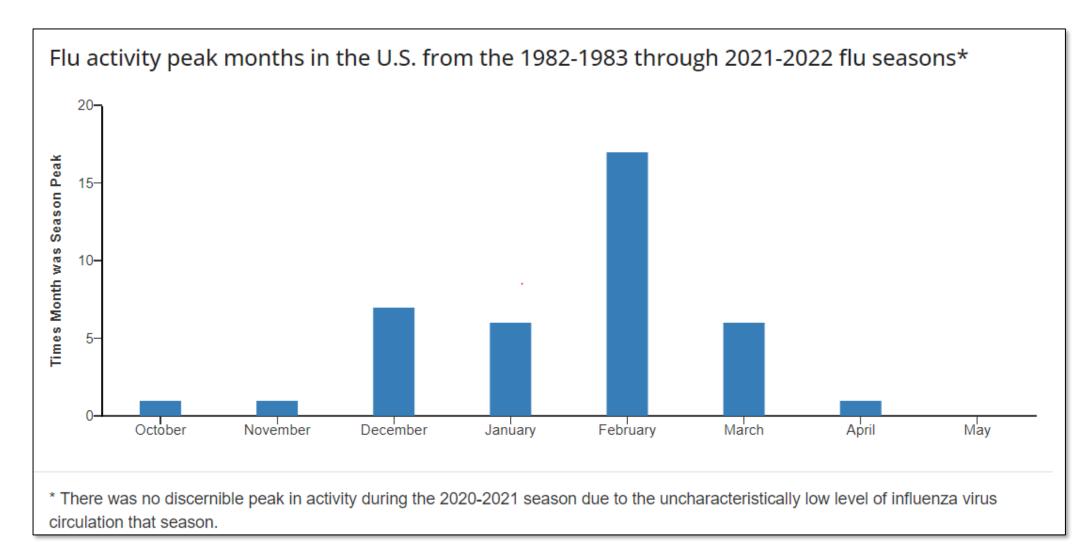
### Influenza Vaccines by Age Indication, United States, 2023–24 Influenza Season

	Vaccine type	0 through 6 months	6 through 23 months	2 through 17 years	18 through 49 years	50 through 64 years	≥65 years
IIV4s	Standard-dose, unadjuvanted inactivated (IIV4)		Afluria Quadrivalent Fluarix Quadrivalent FluLaval Quadrivalent Fluzone Quadrivalent				
	Cell culture-based inactivated (ccIIV4)			Flu	icelvax Quadrivale	nt	
	Adjuvanted inactivated (allV4)						Fluad Quadrivalent
	High-dose inactivated (HD-IIV4)						Fluzone High-Dose Quadrivalent
RIV4	Recombinant (RIV4)					Flublok Quadrival	ent
LAIV4	Live attenuated (LAIV4)			FluMist Qu	ıadrivalent		

**IIV4**=quadrivalent inactivated influenza vaccine **RIV4**=quadrivalent recombinant influenza vaccine **LAIV4**=quadrivalent live attenuated influenza vaccine

Not approved for age group Egg-based Not egg-based

## **Influenza Season Timing**



CDC. The Flu Season. <a href="https://www.cdc.gov/flu/about/season/index.html">https://www.cdc.gov/flu/about/season/index.html</a>

## Waning of Vaccine-Induced Immunity

- Observed in many studies.
  - Variability in rate and degree to which waning occurs across seasons, as well as among different age groups.
  - Most consistently observed among older adults.
  - Noted among children in a few studies.
    - > However, fewer studies provide results for children.
  - In some studies, more pronounced for H3N2 viruses than for H1N1 viruses.
- Variability of results, combined with unpredictability of flu season timing, prevents determination of an ideal time to vaccinate that will generalize across seasons.

## **Timing of Vaccination**

- Vaccination during July and August is not recommended for most groups because of the possible waning of immunity over the course of the influenza season.
- For most persons who need only 1 dose of influenza vaccine for the season,
   vaccination should ideally be offered during September or October.
- However, vaccination should continue after October and throughout the influenza season as long as influenza viruses are circulating and unexpired vaccine is available.

## Timing of Vaccination—2022-23

### Considerations for specific groups:

- Most adults (particularly ages ≥65 years) and pregnant persons in 1st or 2nd trimester: July and August should be avoided unless there is concern that vaccination later in the season might not be possible.
- Children who require 2 doses: Should receive first dose as soon as possible (including during July and August, if vaccine is available) to allow the second dose (which must be administered ≥4 weeks later) to be received, ideally, by the end of October.
- Children who require only 1 dose: Vaccination during July and August can be considered for children of any age who need only 1 dose of influenza vaccine for the season.
  - Not as much evidence for waning as adults (though there are fewer studies including children).
  - Children in the group might visit healthcare providers in late summer.
- **Pregnant persons in 3rd trimester during July/August:** Vaccination during July and August can be considered (can reduce risk for influenza illness in infants during the first months after birth).

# **Benefits of Influenza Vaccination**

## Influenza Vaccine Effectiveness (VE)

- Varies dependent upon factors including
  - Predominant viruses,
  - "Match" between vaccine and circulating viruses,
  - Age and health of recipient.
- Typically greatest in older children and younger adults.
- Tends to be higher in H1N1-predominant seasons than in H3N2-predominant seasons.
- Assessed each season through several CDC networks.

## Estimated Influenza Vaccine Effectiveness (VE), U.S. Flu VE Network

Season	VE, %	95% CI
2011-12	47	(3656)
2012-13	49	(4355)
2013-14	52	(4459)
2014-15	19	(1027)
2015-16	48	(4155)
2016-17	40	(3246)
2017-18	38	(3143)
2018-19	29	(2135)
2019-20	39	(3244)
2021-22	36	(2148)

### Influenza Vaccine "Match" and Vaccine Effectiveness

- Vaccine composition (the viruses that are represented) is considered each year.
  - Composition usually changes each season.
  - Must be determined months in advance (in the U.S., determined in early March).
  - Selection is based on review of global surveillance data.
  - Viruses selected are those anticipated to circulate in the coming season.
  - However, degree of match varies since influenza viruses constantly change.
- During seasons when influenza vaccine viruses are similar to circulating flu viruses, vaccination has been shown to reduce the risk of medically-attended influenza by 40% to 60%.

## **Estimated Annual Influenza Burden Averted through Vaccination**

- Based on annual burden and vaccine effectiveness estimates.
- Substantial burden averted even with modest vaccine effectiveness:
- E.g., for the 2017-18 seasons
  - Vaccine effectiveness: 38%
  - Estimated burden averted:
    - > 5.9 million illnesses
    - 8.2 thousand hospitalizations
    - > 4.8 thousand deaths

Estimated Influenza Illnesses,

Medical Visits, and Hospitalizations

Averted by Vaccination | CDC

From 2010-11 through 2021-22, estimated annual influenza burden averted through vaccination ranged from:

1 to 12 thousand deaths

22 to 100 thousand hospitalizations

1.4 to 7.0 million illnesses

## Thanks!

For more information, contact CDC 1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

